Claims with Markings to Show Changes

At page 1, delete the third paragraph (lines 12-14).

At page 1, line 5, before "Statement" insert the following paragraph:

Reference to Related Applications.

This application is a continuation-in-part of PCT/US98/10080, filed May 15, 1998, which is a continuation-in-part of U.S.S.N. 08/888,534, filed July 7, 1997, and U.S.S.N. 08/857,076, filed May 15, 1997, issued as U.S. Patent No. 6,225,120 on May 1, 2001.

At page 83, replace the second paragraph (lines 14-26) with the following replacement paragraph:

```
Score = 151 (68.4 bits), Expect = 1.9e-140, Sum P(8) = 1.9e-140

Identities = 28/54 (51%), Positives = 38/54 (70%)

SEQ ID NO: 161 AFX:226 SPVGHFAKWSGSPCSRNREEADMWTTFRPRSSSNASSVSTRLSPLRPESEVLAE279

SEQ ID NO: 162 SP F+KW SP S + ++ D W+TFRPR+SSNAS++S RLSP+ E + L E

SEQ ID NO: 163 FKHR:287 SPGSQFSKWPASPGSHSNDDFDNWSTFRPRTSSNASTISGRLSPIMTEQDDLGE340

SEQ ID NO: 164 DAF-16a SFRPRTQSNLSIPGSSS

Score = 132 (59.8 bits), Expect = 1.9e-140, Sum P(8) = 1.9e-140

Identities = 22/42 (52%), Positives = 28/42 (66%)

SEQ ID NO: 165: AFX: 7 KAAAIIDLDPDFEPQSRPRSCTWPLPRPEIANQPSEPPEVEP 48

SEQ ID NO: 166 +A++++DPD FEP RPRSCTWPLPRPE + S P

SEQ ID NO: 167 FKHR: 3 EAPQVVEIDPDFEPLPRPRSCTWPLPRPEFSQSNSATSSPAP 44
```

T ++P+ V ++ D EP+PR R TWP+ RP++ + ++++

SEQ ID NO: 168 DAF-16 TFMNTPDDVMMNDDMEPIPRDRCNTWPMRRPQLEPPLNSSP 177

SEQ ID NO: 169

Beginning at page 97, please replace page 97, second paragraph (lines 3-37), page 98, page 99, and page 100, first paragraph (lines 1-4) with the following replacement paragraphs.

```
Score = 252 (88.7 bits), Expect = 2.2e-60, Sum P(6) = 2.2e-60
Identities = 47/80 (58%), Positives = 60/80 (75%), Frame = +3
SEQ ID NO:170 Query:439 LEKQAGGNPWHQFVENNLILKMGPVDKRKGLFARRRQLLLTEGPHLYYVDPVNKVLKGEI 498
                       LE+Q NP+H F N+LILK G ++K++GLFARRR LLTEGPHL Y+D N VLKGE+
SEQ ID NO:171
SEQ ID NO:172 Sbjct:1818 LEEQRVKNPFHIFTNNSLILKQGYLEKKRGLFARRRMFLLTEGPHLLYIDVPNLVLKGEV1997
SEQ ID NO:170 Query: 499 PWSQELRPEAKNFKTFFVHT 518
SEQ ID NO:171
                        PW+ ++ E KN TFF+HT
SEQ ID NO:172 Sbjct: 1998 PWTPCMQVELKNSGTFFIHT 2057
Score = 201 (70.8 bits), Expect = 2.2e-60, Sum P(6) = 2.2e-60
Identities = 48/123 (39%), Positives = 72/123 (58%), Frame = +1
SEQ ID NO:173 Query: 263 SDLWALGCIIYQLVAGLPPFRAGNEYLIFQKIIKLEYDFPEKFFPKARDLVEKLLVLDAT 322
                       +D+W LGCI++Q +AG PPFRA N+Y + ++I +L++ FPE F +A +++ K+LV
SEQ ID NO: 174
SEQ ID NO:175 Sbjct: 802 TDIWGLGCILFQCLAGQPPFRAVNQYHLLKRIQELDFSFPEGFPEEASEIIAKILV--G*H 978
SEQ ID NO:173 Query: 323 KRLGCE----EMEGYGP------LKAHPFFESVTWENLHQQTPPKLTAYLPAMSEDDE 370
                      + L E ++ P L AH FFE+V W N+ PP L AY+PA
SEQ ID NO:174
SEQ ID NO:175 Sbjct: 979 ETLKTEYVIFNLQVRDPSTRITSQELMAHKFFENVDWVNIANIKPPVLHAYIPATFGEPE1158
SEQ ID NO:173 Query: 371 DCYGN 375
SEQ ID NO:174
SEQ ID NO:175 Sbjct: 1159 -YYSN 1170
Score = 180 (63.4 bits), Expect = 2.2e-60, Sum P(6) = 2.2e-60
Identities = 31/72 (43%), Positives = 52/72 (72%), Frame = +2
SEQ ID NO:176 Query: 157 FGLSYAKNGELLKYIRKIGSFDETCTRFYTAEIVSALEYLHGKGIIHRDLKPENILLNED 216
              F + +NG+L + + GSFD ++F+ +EI++ L++LH I+HRD+KP+N+L+ +D
SEQ ID NO:177
SEQ ID NO:178 Sbjct: 287 FVIGLVENGDLGESLCHFGSFDMLTSKFFASEILTGLQFLHDNKIVHRDMKPDNVLIQKD 466
SEQ ID NO:176 Query: 217 MHIQITDFGTAK 228
SEQ ID NO:177
                         HI ITDFG+A+
SEQ ID NO:178Sbjct: 467 GHILITDFGSAQ 502
Score = 83 (29.2 bits), Expect = 2.2e-60, Sum P(6) = 2.2e-60
Identities = 15/53 (28%), Positives = 32/53 (60%), Frame = +
SEQ ID NO:179 Query:108 YAIKILEKRHIIKENKVPYVTRERDVMSRLD-----HPFFVKLYFTFQDDEKL 155
                      +A+K+L+K ++ + K+ + RE++++ L
                                                     HPF +LY F D ++
SEQ ID NO:180
SEQ ID NO:181 Sbjct: 8 FAVKVLQKSYLNRHQKMDAIIREKNILTYLSQECGGHPFVTQLYTHFHDQARI 166
Score = 81 (28.5 bits), Expect = 2.2e-60, Sum P(6) = 2.2e-60
Identities = 15/29 (51%), Positives = 19/29 (65%), Frame = +2
SEQ ID NO:182 Query: 519 PNRTYYLMDPSGNAHKWCRKIQEVWRQRY 547
                         PNR YYL D
                                    A +WC+ I +V R+RY
SEQ ID NO:183
SEQ ID NO:184 Sbjct: 2129 PNRVYYLFDLEKKADEWCKAINDV-RKRY 2212
```

Score = 78 (27.5 bits), Expect = 2.2e-60, Sum P(6) = 2.2e-60 Identities = 15/25 (60%), Positives = 18/25 (72%), Frame = +3

SEQ ID NO:185
SEQ ID NO:186Query:232
PESKQARANSFVGTAQYVSPELLTE
PE AR +FVGTA YVSPE+L +SEQ ID NO:187Sbjct:660PEENTARRTTFVGTALYVSPEMLAD734

Overall, C. elegans pdk-1 exhibits the following homology to human PDK-1.

Score = 118 (54.4 bits), Expect = 1.4e-104, Sum P(5) = 1.4e-104 Identities = 21/62 (33%), Positives = 41/62 (66%)

SEQ ID NO:188 Query:63 KRTSNDFMFLQSMGEGAYSQVFRCREVATDAMFAVKVLQKSYLNRHQKMDAIIREKNILT 122 K+ DF F + +GEG++S V RE+AT +A+K+L+K ++ + K+ + RE+++++ KKRPEDFKFGKILGEGSFSTVVLARELATSREYAIKILEKRHIIKENKVPYVTRERDVMS 135

 SEQ ID NO:188
 Query:
 123 YL 124

 SEQ ID NO:189
 L

 SEQ ID NO:190
 Sbjct:
 136 RL 137

Score = 230 (106.0 bits), Expect = 1.4e-104, Sum P(5) = 1.4e-104 Identities = 39/90 (43%), Positives = 63/90 (70%)

SEQ ID NO:191 Query: 131 HPFVTQLYTHFHDQARIYFVIGLVENGDLGESLCHFGSFDMLTSKFFASEILTGLQFLHD 190
SEQ ID NO:192 HPF +LY F D ++YF + +NG+L + + GSFD ++F+ +EI++ LH+LH
SEQ ID NO:193 Sbjct: 139 HPFFVKLYFTFQDDEKLYFGLSYAKNGELLKYIRKIGSFDETCTRFYTAEIVSALEYLHG 198

SEQ ID NO:191
SEQ ID NO:192Query:NKIVHRDMKPDNVLIQKDGHILITDFGSAQ
I+HRD+KP+N+L+
KGIIHRDLKPENILLNEDMHIQITDFGTAK
KGIIHRDLKPENILLNEDMHIQITDFGTAK
228

Score = 238 (109.7 bits), Expect = 1.4e-104, Sum P(5) = 1.4e-104 Identities = 43/98 (43%), Positives = 67/98 (68%)

SEQ ID NO:194 Query: 259 EENTARRTTFVGTALYVSPEMLADGDVGPQTDIWGLGCILFQCLAGQPPFRAVNQYHLLK 318
SEQ ID NO:195 E AR +FVGTA YVSPE+L + D+W LGCI++Q +AG PPFRA N+Y + +
SEQ ID NO:196 Sbjct: 233 ESKQARANSFVGTAQYVSPELLTEKSACKSSDLWALGCIIYQLVAGLPPFRAGNEYLIFQ 292

SEQ ID NO:194 Query: 319 RIQELDFSFPEGFPEEASEIIAKILVRDPSTRITSQEL 356
SEQ ID NO:195 +I +L++ FPE F +A +++ K+LV D + R+ +E+
SEQ ID NO:196 Sbjct: 293 KIIKLEYDFPEKFFPKARDLVEKLLVLDATKRLGCEEM 330

Score = 85 (39.2 bits), Expect = 1.4e-104, Sum P(5) = 1.4e-104 Identities = 17/35 (48%), Positives = 21/35 (60%)

SEQ ID NO:197
SEQ ID NO:198Query:356
L AH FFE+V W N+L AY+PA + ESEQ ID NO:199Sbjct:336LKAHPFFESVTWENLHQQTPPKLTAYLPAMSEDDE 370

Score = 324 (149.3 bits), Expect = 1.4e-104, Sum P(5) = 1.4e-104 Identities = 59/104 (56%), Positives = 75/104 (72%)

SEQ ID NO:200 Query: 458 LEEQRVKNPFHIFTNNSLILKQGYLEKKRGLFARRRMFLLTEGPHLLYIDVPNLVLKGEV 517
SEQ ID NO:201 LE+Q NP+H F N+LILK G ++K++GLFARRR LLTEGPHL Y+D N VLKGE+

SEQ ID NO:202 Sbjct: 439 LEKQAGGNPWHQFVENNLILKMGPVDKRKGLFARRRQLLLTEGPHLYYVDPVNKVLKGEI 498

SEQ ID NO:200
SEQ ID NO:201Query:518PWTPCMQVELKNSGTFFIHTPNRVYYLFDLEKKADEWCKAINDV561SEQ ID NO:201PW+ ++ E KN TFF+HTPNR YYL D A +WC+ I +VSEQ ID NO:202Sbjct:499PWSQELRPEAKNFKTFFVHTPNRTYYLMDPSGNAHKWCRKIQEV542

Mapping of the mg142 mutation to this open reading frame establishes the function of this protein. It is much more closely related to PDK than to any other known kinase. PDK is a mammalian kinase that phosphorylates an essential serine residue on AKT, contributing to its activation. The region of akt-1 phosphorylated by PDK-1 is shown below (SEQ ID NO: 203-207, and 305).

SEQ ID NO:203 human AKT 276 KLENLMLDKDGHIKITDFGLCKEGIKDGATMKTFCGTPEYLAPEV 320

KLENL+LDKDGHIKI DFGLCKE I G TFCGTPEYLAPEV

SEQ ID NO:205 Ce akt-1 33509 KLENLLLDKDGHIKIADFGLCKEEISFGDKTSTFCGTPEYLAPEV 33643

SEQ ID NO:206 Ceakt2 326 LCKEEIKYGDKTSTFCGTPEYLAPEVIEDIDYDRSVDWWGVGVVMYEMMCGRLPFSAKENGK
SEQ ID NO:207 LCKE I G TFCGTPEYLAPEV+ED DYR+VDWWG+GVVMYEMMCGRLPF +++ +

SEQ ID NO:305 MOAKT: 298 LCKEGISDGATMKTFCGTPEYLAPEVLEDNDYGRAVDWWGLGVVMYEMMCGRLPFYNQDHER

Replace page 178, fourth paragraph, lines 21-24, page 179-186, and page 187, first paragraph, lines 1-14, with the following replacement paragraphs:

Pepck

>R11A5 Length = 26,671Plus Strand HSPs: Score = 994 (461.5 bits), Expect = 0.0, Sum P(5) = 0.0Identities = 176/223 (78%), Positives = 195/223 (87%), Frame = +1SEQ ID NO:211 Query:201 AKNNGEFVRCVHSVGQPKPVATKVINHWPCNPEKTIIAHRPAEREIWSFGSGYGGNSLLG 260 SEQ ID NO:212 A N +FVRC+HSVG P+PV +VINHWPCNPE+ +IAHRP EREIWSFGSGYGGNSLLG SEQ ID NO:213Sbjct:8682 ALGNQDFVRCIHSVGLPRPVKQRVINHWPCNPERVLIAHRPPEREIWSFGSGYGGNSLLG 18861 SEQ ID NO:211 Query: 261 KKCFALRIAMNIGYDEGWMAEHMLIMGVTSPKGEERFVAAAFPSACGKTNLAMLEPTIPG 320 SEQ ID NO:212 KKCFALRIA NI DEGWMAEHMLIMGVT P G E F+AAAFPSACGKTNLAMLEPT+PG SEQ ID NO:213 Sbjct:18862 KKCFALRIASNIAKDEGWMAEHMLIMGVTRPCGREHFIAAAFPSACGKTNLAMLEPTLPG 19041 SEQ ID NO:211 Query: 321 WKVRVIGDDIAWMKFGADGRLYAINPEYGFFGVAPGTSHKTNPMAMASFQENTIFTNVAE 380 SEQ ID NO:212 WKVR +GDDIAWMKFG DGRLYAINPE GFFGVAPGTS+KTNPMA+A+FQ+N+IFTNVAE SEQ ID NO:213 Sbjct:19042 WKVRCVGDDIAWMKFGEDGRLYAINPEAGFFGVAPGTSNKTNPMAVATFQKNSIFTNVAE 19221 SEQ ID NO:211 Query: 381 TADGEYFWEGLEHEVKNPKVDMINWLGEPWHIGDESKAAHPNS 423 SEQ ID NO:212 TA+GEYFWEGLE E+ + VD+ WLGE WHIG+ SEQ ID NO:213 Sbjct: 19222 TANGEYFWEGLEDEIADKNVDITTWLGEKWHIGEPGVAAHPNS 19350 Score = 657 (305.1 bits), Expect = 0.0, Sum P(5) = 0.0Identities = 120/173 (69%), Positives = 144/173 (83%), Frame = +1

SEQ ID NO:214 Query: 32 KGDFVSLPKHVQRFVAEKAELMKPSAIFICDGSQNEADELIARCVERGVLVPLKAYKNNY 91 SEQ ID NO:215 +GDF LP VQRF+AEKAELM+P IFICDGSQ+EADELI + +ERG+L L+AY+NNY SEQ ID NO:216 Sbjct:18181 QGDFHLLPAKVQRFIAEKAELMRPRGIFICDGSQHEADELIDKLIERGMLSKLEAYENNY 18360 SEQ ID NO:214 Query: 92 LCRTDPRDVARVESKTWMITPEKYDSVCHTPEGVKPMMGQWMSPDEFGKELDDRFPGCMA 151 +CRTDP+DVARVESKTWM+T KYD+V HT EGV+P+MG W++P++ ELD RFPGCMA SEQ ID NO:215 SEQ ID NO:216 Sbjct:183611CRTDPKDVARVESKTWMVTKNKYDTVTHTKEGVEPIMGHWLAPEDLATELDSRFPGCMA 18540 SEQ ID NO:214 Query: 152 GRTMYVIPYSMGPVGGPLSKIGIELTDSDYVVLCMRIMTRMGEPVLKALAKNN 204 SEQ ID NO:215 GR MYVIP+SMGPVGGPLSKIGI+LTDS+YVVL MRIMTR+ V AL SEQ ID NO:216 Sbjct: 18541 GRIMYVIPFSMGPVGGPLSKIGIQLTDSNYVVLSMRIMTRVNNDVWDALGNQD 18699 Score = 453 (210.3 bits), Expect = 0.0, Sum P(5) = 0.0 Identities = 77/107 (71%), Positives = 90/107 (84%), Frame = +1 SEQ ID NO:217 Query: 424 RFTAPAGQCPIIHPDWEKPEGVPIDAIIFGGRRPEGVPLVFESRSWVHGIFVGACVKSEA 483 SEQ ID NO:218 RF APA QCPIIHPDWE P+GVPI+AIIFGGRRP+GVPL++E+ SW HG+F G+C+KSEA SEQ ID NO:219 Sbjct:19396 RFAAPANQCPIIHPDWESPQGVPIEAIIFGGRRPQGVPLIYETNSWEHGVFTGSCLKSEA 19575 SEQ ID NO:217 Query: 484 TAAAEHTGKQVMHDPMAMRPFMGYNFGRYMRHWMKLGQPPHKVPKIF 530 SEO ID NO:218 TAAAE TGK VMHDPMAMRPFMGYNFG+Y++HW+ L SEQ ID NO:219 Sbjct: 19576 TAAAEFTGKTVMHDPMAMRPFMGYNFGKYLQHWLDLKTDSRKVIDFF 19716 Score = 404 (187.6 bits), Expect = 0.0, Sum P(5) = 0.0Identities = 68/116 (58%), Positives = 89/116 (76%), Frame = +1SEQ ID NO: 220 Query: 526 VPKIFHVNWFRQSADHKFLWPGYGDNIRVIDWILRRCSGDATIAEETPIGFIPKKGTINL585 SEQ ID NO:221 +PKI+HVNWFR+ +++KFLWPG+GDNIRVIDWI+RR G+ I ETPIG +P KG+INL SEQ ID NO:222 Sbjct: 19750 MPKIYHVNWFRKDSNNKFLWPGFGDNIRVIDWIIRRLDGEQEIGVETPIGTVPAKGSINL 19929 SEQ ID NO:220 Query: 586 EGLPNVNWDELMSIPKSYWLEDMVETKTFFENQVGSDLPPEIAKELEAQTERIKAL 641 SEQ ID NO:221 EGL VNWDELMS+P YW +D E + F + QVG DLP + E++AQ +R++ L SEQ ID NO:222 Sbjct: 19930 EGLGEVNWDELMSVPADYWKQDAQEIRKFLDEQVGEDLPEPVRAEMDAQEKRVQTL 20097 Score = 69 (32.0 bits), Expect = 0.0, Sum P(5) = 0.0Identities = 15/36 (41%), Positives = 21/36 (58%), Frame = +1 SEQ ID NO:223 Query: 5 SLSHFKDDDFAVVSEVVTHKQNHIPVIKGDFVSLPK 40 SEQ ID NO:224 SL +D F VV+EVV + H+P++K F S K SEQ ID NO:225 Sbjct: 14722 SLRQISEDAFYVVNEVVMKRLGHVPILKVIFESSEK 14829 Score = 39 (18.1 bits), Expect = 6.9e-244, Sum P(4) = 6.9e-244Identities = 9/25 (36%), Positives = 11/25 (44%), Frame = +3SEQ ID NO:226 Query: 148 GCMAGRTMYVIPYSMGPVGGPLSKI 172 SEQ ID NO:227 GC R + V P S PL K+ SEQ ID NO:228 Sbjct: 8040 GCSGRRVLCVCPCSHSSSALPLQKV 8114 Score = 38 (17.6 bits), Expect = 4.0e-285, Sum P(5) = 4.0e-285Identities = 7/16 (43%), Positives = 9/16 (56%), Frame = +1 SEQ ID NO:229 Query: 588 LPNVNWDELMSIPKSY 603 SEQ ID NO:230 L + NW +S P SY SEQ ID NO:231 Sbjct: 22654 LESFNWFSFVSCPDSY 22701 Score = 37 (17.2 bits), Expect = 2.0e-48, Sum P(3) = 2.0e-48Identities = 6/14 (42%), Positives = 9/14 (64%), Frame = +1

SEQ ID NO:232 Query: 117 SVCHTPEGVKPMMG 130

<u>SEQ ID NO:233</u> <u>SEQ ID NO:234</u> Sbjct: 19603 TVMHDPMAMRPFMG 19644

Acetyl coa carboxylase

>W09B6

Length = 32,900

Plus Strand HSPs:

Score = 562 (259.1 bits), Expect = 0.0, Sum P(14) = 0.0 Identities = 109/197 (55%), Positives = 138/197 (70%), Frame = +2

SEQ ID NO:235 Query: 1951 SGFFDYGSFSEIMQPWAQTVVVGRARLGGIPVGVVAVETRTVELSVPADPANLDSEAKII 2010
SEQ ID NO:236 z +G D SF EI WA+++V GRARL GIP+GVV+ E R VPADPA S+ +
SEQ ID NO:237 Sbjct:28280 TGICDTMSFDEICGDWAKSIVAGRARLCGIPIGVVSSEFRNFSTIVPADPAIDGSQVQNT 28459

SEQ ID NO:235 Query: 2011 QQAGQVWFPDSAFKTYQAIKDFNREGLPLMVFANWRGFSGGMKDMYDQVLKFGAYIVDGL 2070 Q+AGQVW+PDSAFKT +AI D N+E LPLM+ A+ RGFSGG KDMYD VLKFGA IVD L SEQ ID NO:237 Sbjct:28460 QRAGQVWYPDSAFKTAEAINDLNKENLPLMIIASLRGFSGGQKDMYDMVLKFGAQIVDAL 28639

SEQ ID NO:235 Query: 2071 RECSQPVMVYIPPQAELRGGSWVVIDPTINPRHMEMYADRESRGSVLEPEGTVEIKFRKK 2130
SEQ ID NO:236 ++PV+VYIP ELRGG+W V+D I P + + AD +SRG +LEP V IKFRK
SEQ ID NO:237 Sbjct: 28640 AVYNRPVIVYIPEAGELRGGAWAVLDSKIRPEFIHLVADEKSRGGILEPNAVVGIKFRKP 28819

 SEQ ID NO:235
 Query:
 2131
 DLVKTMRRVDPVYIRLA
 2147

 SEQ ID NO:236
 +++ M+R DP Y +L+

SEQ ID NO:237 Sbjct: 28820 MMMEMMKRSDPTYSKLS 28870

Score = 357 (164.6 bits), Expect = 0.0, Sum P(14) = 0.0Identities = 68/124 (54%), Positives = 89/124 (71%), Frame = +2

SEQ ID NO:238 Query:303 VGYPVMIKASEGGGGKGIRKVNNADDFPNLFRQVQAEVPGSPIFVMRLAKQSRHLEVQIL 362
SEQ ID NO:239 +G+P+MIKASEGGGGKGIRK +DF +FF +V EV GSPIF+M+ +RH+EVQ+L
SEQ ID NO:240 Sbjct:23264IGFPLMIKASEGGGGKGIRKCTKVEDFKSMFEEVAQEVQGSPIFLMKCVDGARHIEVQLL 23443

SEQ ID NO:238 Query: 363 ADQYGNAISLFGRDCSVQRRHQKXXXXXXXXXXXXXXVFEHMEQCAVKLAKMVGYVSAGTV 422

SEQ ID NO:239 AD+Y N IS++ RDCS+QRR QK + + M++ AV+LAK VGY SAGTV 5EQ ID NO:240 Sbjct:23444ADRYENVISVYTRDCSIQRRCQKIIEEAPAIIASSHIRKSMQEDAVRLAKYVGYESAGTV 23623

 SEQ ID NO:238
 Query:
 423
 EYLY 426

 SEQ ID NO:239
 EYLY
 EYLY

 SEQ ID NO:240
 Sbjct:
 23624
 EYLY 23635

Score = 345 (159.1 bits), Expect = 0.0, Sum P(14) = 0.0Identities = 65/116 (56%), Positives = 86/116 (74%), Frame = +2

SEQ ID NO:241 Query:1787 KEEGLGAENLRGSGMIAGESSLAYDEIITISLVTCRAIGIGAYLVRLGQRTIQVENSHLI 1846
SEQ ID NO:242 K E +G ENL+GSG+IAGE++ AY E+ T VT R++GIGAY RL R +Q + SHLI
SEQ ID NO:243 Sbjct:27794 KNEKIGVENLQGSGLIAGETARAYAEVPTYCYVTGRSVGIGAYTARLAHRIVQHKQSHLI 27973

SEQ ID NO:241 Query: 1847 LTGAGALNKVLGREVYTSNNQLGGIQIMHNNGVTHCTVCDDFEGVFTVLHWLSYMP 1902
SEQ ID NO:242 LTG ALN +LG++VYTSNNQLGG ++M NGVTH V +D EG+ V+ W+S++P
SEQ ID NO:243 Sbjct: 27974 LTGYEALNTLLGKKVYTSNNQLGGPEVMFRNGVTHAVVDNDLEGIAKVIRWMSFLP 28141

Score = 319 (147.1 bits), Expect = 0.0, Sum P(14) = 0.0Identities = 59/119 (49%), Positives = 80/119 (67%), Frame = +2

```
SEQ ID NO:244 Query: 503 HVIAARITSENPDEGFKPSSGTVQELNFRSNKNVWGYFSVAAAGGLHEFADSQFGHCFSW 562
SEQ ID NO:245
                         H IAARIT ENPD+ F+PS+G V E+NF S+++ W YFSV
                                                                    +H+FADSOFGH F+
SEQ ID NO:246 Sbjct:23870 HAIAARITCENPDDSFRPSTGKVYEINFPSSQDAWAYFSVGRGSSVHQFADSQFGHIFTR 24049
SEQ ID NO:244 Query:
                       563 GENREEAISNMVVALKELSIRGDFRTTVEYLIKLLETESFQLNRIDTGWLDRLIAEKVQ 621
SEQ ID NO:245
                           G +R EA++ M
                                       LK ++IR F T V YL+ L+ F N +T WLD+ IA K++
SEQ ID NO:246 Sbjct: 24050 GTSRTEAMNTMCSTLKHMTIRSSFPTQVNYLVDLMHDADFINNAFNTQWLDKRIAMKIK 24226
Score = 303 (139.7 bits), Expect = 0.0, Sum P(14) = 0.0
Identities = 55/90 (61%), Positives = 70/90 (77%), Frame = +2
SEQ ID NO: 247 Query:
                        178 PGGANNNYANVELILDIAKRIPVQAVWAGWGHASENPKLPELLLKNGIAFMGPPSQAMW 237
SEQ ID NO: 248
                            P G N NN+ANV+ IL A + V AVWAGWGHASENP LP L + IAF+GPP+ AM+
SEQ ID NO: 249 Sbjct: 22886 PSGTNKNNFANVDEILKHAIKYEVDAVWAGWGHASENPDLPRRLNDHNIAFIGPPASAMF 23065
SEQ ID NO: 247 Query:
                       238 ALGDKIASSIVAQTAGIPTLPWSGSGLRVD 267
SEQ ID NO: 248
                            +LGDKIAS+I+AQT G+PT+ WSGSG+ ++
SEQ ID NO: 249 Sbjct: 23066 SLGDKIASTIIAQTVGVPTVAWSGSGITME 23155
Trehelase
>C23H3
  Length = 39,721
  Minus Strand HSPs:
Score = 227 (104.5 bits), Expect = 1.0e-95, Sum P(6) = 1.0e-95
Identities = 36/67 (53%), Positives = 51/67 (76%), Frame = -2
SEQ ID NO:250 Query:
                     2 VIKNLGYMVDNHGFVPNGGRVYYLTRSQPPLLTPMVYEYYMSTGDLDFVMEILPTLDKEY 61
SEQ ID NO:251
                         +I N +++++ GFVPNGGRVYYL RSQPP PMVYEYY++T D+ V +++P ++KEY
SEQ ID NO:252 Sbjct:9798 MILNFAHIIETYGFVPNGGRVYYLRRSQPPFFAPMVYEYYLATQDIQLVADLIPVIEKEY 9619
SEQ ID NO:250 Query:
                       62 EFWIKNR 68
SEQ ID NO:251
                          FW + R
SEQ ID NO:252 Sbjct: 9618 TFWSERR 9598
Score = 182 (83.8 bits), Expect = 1.0e-95, Sum P(6) = 1.0e-95
Identities = 32/92 (34%), Positives = 55/92 (59%), Frame = -2
SEQ ID NO: 253 Query: 146 MDSIRTWSIIPADLNAFMCANARILASLYEIAGDFKKVKVFEQRYTWAKREMRELHWNET 205
SEQ ID NO:254
                         + +I T +I+P DLNAF+C N I+ Y++ G+ K + R+T +
SEQ ID NO:255 Sbjct: 9372
                            ISTIETTNIVPVDLNAFLCYNMNIMQLFYKLTGNPLKHLEWSSRFTNFREAFTKVFYVPA 9193
SEQ ID NO:253 Query: 206 DGIWYDYDIELKTHSNQYYVSNAVPLYAKCYD 237
SEO ID NO:254
                            WYDY++
                                    TH+ ++ SNAVPL+++CYD
SEQ ID NO:255 Sbjct: 9192 RKGWYDYNLRTLTHNTDFFASNAVPLFSQCYD 9097
Score = 178 (81.9 bits), Expect = 1.0e-95, Sum P(6) = 1.0e-95
Identities = 37/102 (36%), Positives = 55/102 (53%), Frame = -2
SEQ ID NO:256 Query:
                     246 VHDYLERQGLLKYTKGLPTSLAMSSTQQWDKENAWPPMIHMVIEGFRTTGDIKLMKVAEK 305
SEQ ID NO:257
                                       G+PTS+ + QQWD N W PM HM+IEG R + + L + A
                         V++ ++ G
SEQ ID NO:258 Sbjct: 9069 VYNEMQNSGAFSIPGGIPTSMNEETNQQWDFPNGWSPMNHMIIEGLRKSNNPILQQKAFT 8890
SEQ ID NO:256 Query:
                     306 MATSWLTGTYQSFIRTHAMFEKYNVTPHTEETSGGGGGEYEV 347
SEQ ID NO:257
                         +A WL O+F + M+EKYNV
                                                     + + GG E +V
```

SEQ ID NO:258 Sbjct: 8889 LAEKWLETNMQTFNVSDEMWEKYNVKEPLGKLATGGEYEVQV 8764

Score = 169 (77.8 bits), Expect = 1.0e-95, Sum P(6) = 1.0e-95 Identities = 29/58 (50%), Positives = 41/58 (70%), Frame = -2

SEQ ID NO:259 Query: 84 YQYKAKLKVPRPESYREDSELAEHLQTEAEKIQMWSEIASAAETGWDFSTRWFSQNGD 141
SEQ ID NO:261 Sbjct: 9546 FQYRTEAETPRPESFREDVLSAEHFTTKDRKKQFFKDLGSAAESGWDFSSRWFKNHKD 9373

Score = 76 (35.0 bits), Expect = 1.0e-95, Sum P(6) = 1.0e-95 Identities = 13/21 (61%), Positives = 15/21 (71%), Frame = -1

 SEQ ID NO:262
 Query:
 348 QTGFGWTNGVILDLLDKYGDQ 368

 SEQ ID NO:264
 Sbjct:
 8722 QAGFGWTNGAALDLIFTYSDR 8660

Score = 45 (20.7 bits), Expect = 1.0e-95, Sum P(6) = 1.0e-95 Identities = 10/24 (41%), Positives = 15/24 (62%), Frame = -1

 SEQ ID NO:265
 Query:
 371
 SSSTASKFSFSLSNITFVVFILYI
 394

 SEQ ID NO:266
 +SS++S F +S VF+LYI

 SEQ ID NO:267
 Sbjct:
 8545
 TSSSSSTFGYSNILTLITVFVLYI
 8474

Score = 38 (17.5 bits), Expect = 2.6e-98, Sum P(7) = 2.6e-98 Identities = 7/7 (100%), Positives = 7/7 (100%), Frame = -2

 SEQ ID NO:268
 Query:
 342 GGEYEVQ 348

 SEQ ID NO:269
 GGEYEVQ GGEYEVQ 8767

 SEQ ID NO:270
 Sbjct:
 8787 GGEYEVQ 8767

Score = 37 (17.0 bits), Expect = 1.6e-19, Sum P(4) = 1.6e-19 Identities = 8/18 (44%), Positives = 10/18 (55%), Frame = -2

 SEQ ID NO:271
 Query:
 217
 KTHSNQYYVSNAVPLYAK
 234

 SEQ ID NO:272
 K ++ YYVS P Y K

 SEQ ID NO:273
 Sbjct:
 30345
 KFTAHPYYVSRTPPRYHK
 30292

>W05E10

Length = 31,273

Minus Strand HSPs:

Score = 224 (103.1 bits), Expect = 7.0e-90, Sum P(7) = 7.0e-90 Identities = 43/67 (64%), Positives = 49/67 (73%), Frame = -1

SEQ ID NO:274 Query: 2 VIKNLGYMVDNHGFVPNGGRVYYLTRSQPPLLTPMVYEYYMSTGDLDFVMEILPTLDKEY 61
SEQ ID NO:275 +I+NL MVD +GFVPNGGRVYYL RSQPP L MVYE Y+ T D FV E+LPTL KE
SEQ ID NO:276Sbjct:28957MIRNLASMVDKYGFVPNGGRVYYLQRSQPPFLAAMVYELYEATNDKAFVAELLPTLLKEL28778

 SEQ ID
 NO:274
 Query:
 62
 EFWIKNR
 68

 SEQ ID
 NO:275
 FW + R

 SEQ ID
 NO:276
 Sbjct:
 28777
 NFWNEKR
 28757

Score = 192 (88.4 bits), Expect = 7.0e-90, Sum P(7) = 7.0e-90 Identities = 31/84 (36%), Positives = 52/84 (61%), Frame = -3

SEQ ID NO:277 Query: 154 IIPADLNAFMCANARILASLYEIAGDFKKVKVFEQRYTWAKREMRELHWNETDGIWYDYD 213

SEQ ID NO:278 ++P DLN + C N I + LYE GD K ++F + + ++ + +N TDG WYDY+ SEQ ID NO: 279 Sbjct: 2842 7VLPVDLNGLLCWNMDIMEYLYEQIGDTKNSQIFRNKRADFRDTVQNVFYNRTDGTWYDYN 28248 SEQ ID NO:277 Query: 214 IELKTHSNQYYVSNAVPLYAKCYD 237 SEO ID NO:278 + ++H+ ++Y S AVPL+ CY+ SEQ ID NO:279 Sbjct: 28247 LRTQSHNPRFYTSTAVPLFTNCYN 28176 Score = 125 (57.5 bits), Expect = 7.0e-90, Sum P(7) = 7.0e-90Identities = 20/48 (41%), Positives = 30/48 (62%), Frame = -2SEQ ID NO 280 Query: 249 YLERQGLLKYTKGLPTSLAMSSTQQWDKENAWPPMIHMVIEGFRTTGD 296 SEQ ID NO 281 + ++ G+ Y G+PTS++ S QQWD N W P HM+IEG R + + SEQ ID NO 282 Sbjct: 28092 FFQKMGVFTYPGGIPTSMSQESDQQWDFPNGWSPNNHMIIEGLRKSAN 27949 Score = 90 (41.4 bits), Expect = 7.0e-90, Sum P(7) = 7.0e-90Identities = 15/18 (83%), Positives = 18/18 (100%), Frame = -2SEQ ID NO 283 Query: 120 EIASAAETGWDFSTRWFS 137 SEQ ID NO 284 ++ASAAE+GWDFSTRWFS SEQ ID NO 285 Sbjct: 28566 DLASAAESGWDFSTRWFS 28513 Score = 89 (41.0 bits), Expect = 7.0e-90, Sum P(7) = 7.0e-90Identities = 18/40 (45%), Positives = 24/40 (60%), Frame = -1SEQ ID NO 286 Query: 79 KQFPYYQYKAKLKVPRPESYREDSELAEHLQTEAEKIQMW 118 SEQ ID NO 287 K F YOYK VPRPESYR D++ + L A++ Q + SEQ ID NO 288 Sbjct: 28732 KSFKVYQYKTASNVPRPESYRVDTQNSAKLANGADQQQFY 28613 Score = 77 (35.4 bits), Expect = 7.0e-90, Sum P(7) = 7.0e-90Identities = 14/21 (66%), Positives = 16/21 (76%), Frame = -3SEQ ID NO 289 Query: 348 QTGFGWTNGVILDLLDKYGDQ 368 SEQ ID NO 290 Q GFGW+NG ILDLL Y D+ SEQ ID NO 291 Sbjct: 24395 QDGFGWSNGAILDLLLTYNDR 24333 Score = 51 (23.5 bits), Expect = 7.0e-90, Sum P(7) = 7.0e-90Identities = 11/27 (40%), Positives = 16/27 (59%), Frame = -3SEQ ID NO 292 Query: 365 YGDQFASSSTASKFSFSLSNITFVVFI 391 SEQ ID NO 293 Y FASSS AS FS +++ F + + SEQ ID NO 294 Sbjct: 2846 YN*PFASSSDASSCPFSTNSVIFSILV 2766 Score = 41 (18.9 bits), Expect = 3.3e-93, Sum P(8) = 3.3e-93Identities = 7/9 (77%), Positives = 8/9 (88%), Frame = -2SEQ ID NO 295 Query: 340 GGGGEYEVQ 348 SEQ ID NO 296 G GGEY+VQ SEQ ID NO 297 Sbjct: 24468 GSGGEYDVQ 24442 Score = 39 (18.0 bits), Expect = 2.0e-37, Sum P(5) = 2.0e-37Identities = 7/14 (50%), Positives = 8/14 (57%), Frame = -2SEQ ID NO 298 Query: 221 NQYYVSNAVPLYAK 234 SEQ ID NO 299 N YY+ V LY K SEQ ID NO 300 Sbjct: 4524 NHYYIIQMVSLYTK 4483

Score = 38 (17.5 bits), Expect = 4.0e-88, Sum P(7) = 4.0e-88 Identities = 11/30 (36%), Positives = 13/30 (43%), Frame = -1

 SEQ ID NO 301
 Query:
 367
 DQFASSSTASKFSFSLSNITFVVFILYIFS
 396

 SEQ ID NO 302
 DQF S SKFS + F +FS

 SEQ ID NO 303
 Sbjct:
 7588
 DQFVISFICSKFSSKNKKLYFCPSHFSLFS
 7499

In the Claims:

- 1. (Twice Amended) A method for identifying a compound that modulates DAF-18 expression or activity, comprising:
- (a) providing a nematode, isolated nematode cell, or isolated mammalian cell expressing a nematode daf-18 gene; and
- (b) contacting said nematode, isolated nematode cell, or isolated mammalian cell with a candidate compound[, an alteration in] to determine the effect of said candidate compound on daf-18 expression or activity, an alteration in said daf-18 expression or activity following contact of said nematode, isolated nematode cell, or isolated mammalian cell with said candidate compound identifying said candidate compound as a modulatory compound.
- 2. (Twice Amended) A method for identifying a compound that modulates PTEN expression or activity, comprising:
- (a) providing a nematode or isolated nematode cell comprising a mutation in its endogenous *daf-18* gene;
- (b) expressing in said nematode or isolated nematode cell a mammalian PTEN gene; and
- (c) contacting said nematode or isolated nematode cell with a candidate compound[, an alteration in] to determine the effect of said candidate compound on PTEN expression or activity, an alteration in said PTEN expression or activity following contact with said candidate compound identifying said candidate compound as a modulatory compound.